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09/772,445	01/29/2001	Hynda K. Kleinman	2600-109	1045

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EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
12/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	09/772,445	KLEINMAN ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40,53-61,133-136,173-176 and 178-186* is/are pending in the application.

4a) Of the above claim(s) *9,10,12,20,21,31,32,37,40,56 and 178-182* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11,13-19,22-30,33-36,38,39,53-55,57-61,133-136,173-176,183-186* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendments and arguments filed 8/31/09 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Previously, applicant elected group 1 (claims 1-40,47-49,53-61,133-136) (11/5/04) and elected a species comprising amino acids LKKTET (2/24/05) for the would healing polypeptide. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Due to the addition of new claims an additional election of species requirement was sent 1/6/09.

Applicant's election of the following species:

Patient population: skin wound

Further agent: transforming growth factor beta

Further excipient: sterile water

in the reply filed on 2/5/09 is acknowledged.

Claims 41-52,62-132,137-172,177 have been cancelled.

Claims 178-182 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/5/04.

Claims 9-10,12,20-21,31-32,37,40,56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/5/09.

In particular, claims 9-10,20-21 are to a species of wound healing polypeptide other than LKKTET. Claims 12,31-32,37 are to a species of further agent other than transforming growth factor beta. Claims 40,56 are to a patient population other than skin wound.

In the instant case, each of the elected species were found in the prior art. Any art that was found in the course of searching for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP the Markush-type claims and the claims to the elected species are rejected and claims to the nonelected species are held withdrawn from consideration.

Claims 1-8,11,13-19,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186 are under consideration.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-

filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/094,690 (7/30/98), fails to provide adequate written description in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In the instant case, Claims 1-8,11,13,16-18,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186 refer to the amino acid sequence LKKTET or to isoforms.

Lack of Ipsis Verbis Support

Application No. 60/094,690 (7/30/98), is void of support for the amino acid sequence LKKTET or for isoforms.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to new claim limitations, the analysis is similar in determining conditions for receiving the benefit of an earlier filing date.

Application No. 60/094,690 (7/30/98), does recite thymosin beta 4. However, the disclosure of thymosin beta 4 would not lead one to the sequence LKKTET or to isoforms. For at least these reasons, one would not conclude that Application No. 60/094,690 provides adequate support for Claims 1-8,11,13,16-18,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186.

The disclosure of the prior-filed application, PCT/US99/17282 (7/29/99), fails to provide adequate written description in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

In the instant case, Claim 136 recites 'lactated Ringer's intravenous polyalklene glycol'. Claims 173-176 are drawn to ranges of at least 0.01 ng/ml and up to 60 ug per 300 microliter.

Lack of Ipsis Verbis Support

PCT/US99/17282 is void of support for 'lactated Ringer's intravenous polyalklene glycol'. PCT/US99/17282 is void of support for 'at least 0.01 ng/ml and up to 60 ug per 300 microliter'. PCT/US99/17282 is void of support for the word 'neuron'.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

Although the above statement is with respect to new claim limitations, the analysis is similar in determining conditions for receiving the benefit of an earlier filing date.

PCT/US99/17282 refers to Ringer's intravenous vehicles. However, such disclosure does not lead one to 'lactated Ringer's intravenous polyalklene glycol' of claim 136.

PCT/US99/17282 (figures 6-7) shows specific concentrations of thymosin beta 4 used in a particular assay. However, there is no support for any and all ranges in between to particular amounts. Further, it appears that disparate sections of the specification have been used to come up with the ranges recited in the claims. It is noted that claims 173-176 depend from claims

1,13,23,53 respectively. However, one would not have necessarily recognized the use of the instantly claimed ranges for applications of claims 1,13,23,53.

For at least these reasons, one would not conclude that PCT/US99/17282 provides adequate support for Claims 136,173-176.

It is noted that section 706.02 VI D of the MPEP sets forth the method to determine the effective filing date. In particular, 'If the application properly claims benefit under 35 U.S.C. 119(e) to a provisional application, the effective filing date is the filing date of the provisional application for any claims which are fully supported under the first paragraph of 35 U.S.C. 112 by the provisional application.'. It is noted that claims are either fully supported or not fully supported. In other words, claims are not treated as 'supported in part' even though one particular element may be supported in the provisional application. In the instant case, claims 14-15,19 are searched based on a priority date of 7/30/98. Claims 1-8,11,13,16-18,22-30,33-36,38-39,53-55,57-61,133-135 are searched based on a priority date of 7/29/99.

Response to Arguments – Priority (60/094,690)

Applicants argue (page 20) that isoforms and the LKKTET motif were well known at the time the priority application was filed.

Applicant's arguments filed 8/31/09 have been fully considered but they are not persuasive.

Although Applicants argue (page 20) that isoforms and the LKKTET motif were well known at the time the priority application was filed, what is known in the art is not necessarily express, implicit, or inherent support for the instant claims. Applicants have not provided any evidence that knowledge, coupled with Applicant disclosure, provided express, implicit or

inherent support for the claimed invention. Applicants have not cited the pages within the provisional where such support can be found. Application No. 60/094,690 (7/30/98), does recite thymosin beta 4. However, the disclosure of thymosin beta 4 would not lead one to the sequence LKKTET or to isoforms. There is no reason to interpret thymosin beta 4 to mean only a particular fragment or isoform thereof.

Response to Arguments – Priority (PCT/US99/17282)

Applicants argue (pages 20-21) that the reference discloses lactated Ringers intravenous vehicles as well as polyalkylene glycols.

Applicants argue that since certain dosages work then one would recognize ranges.

Applicant's arguments filed 8/31/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 20-21) that the reference discloses lactated Ringers intravenous vehicles as well as polyalkylene glycols, the claims recite 'lactated Ringer's intravenous polyalklene glycol'. The disclosure of lactated Ringers intravenous vehicles is generic and would not lead one to polyalklene glycol. Although polyalklene glycol is mentioned, it is from a disparate section of the reference and there is no reason to read in that polyalklene glycol is intended to be lactated Ringer's intravenous polyalklene glycol.

Although argue that since certain dosages work then one would recognize ranges, disparate sections of the specification have been used to come up with the ranges recited in the claims. A disclosure of 2 data points does not lead one to any and all ranges in between those data points.

Claim Rejections - 35 USC § 112

This 112 2nd rejection is necessitated by applicants amendments to claims 1,23.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2,5-8,11,23-28,33-36,38-39,133-136,173,175,183-184 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1,23 and dependent claims 2,5-8,11,24-28,33-36,38-39,133-136,173,175,183-184 recite 'replaced with another hydrophobic amino and residue'. Such phrase is unclear and the scope of the isoforms is unclear. The phrase is open to multiple interpretations. It appears that the intent is to define the scope of possibilities for the replacement. However, the structure of a 'hydrophobic amino and residue' is unclear. Although the art recognizes 'hydrophobic amino acids', the instant phrase 'hydrophobic amino' is unclear. Further, it is unclear if 'and residue' is meant to be another residue and if so the nature of such residue is unclear.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements. Due to the lack of clarity an updated art search was performed.

Claims 136,173-176 were previously rejected. Since the claims have been amended, the rejection has been updated to correspond to the instant claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 136,173-176 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, Claim 136 recites 'lactated Ringer's intravenous polyalklene glycol'. Claims 173-176 are drawn to ranges of at least 0.01 ng/ml and up to 60 ug per 300 microliter.

Lack of Ipsis Verbis Support

The specification is void of literal support for 'lactated Ringer's intravenous polyalklene glycol'. The specification is void of literal support for 'at least 0.01 ng/ml and up to 60 ug per 300 microliter'.

Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: 'While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'.

The specification refers to Ringer's intravenous vehicles. However, such disclosure does not lead one to 'lactated Ringer's intravenous polyalklene glycol' of claim 136.

The specification (figures 6-7) shows specific concentrations of thymosin beta 4 used in a particular assay. However, there is no support for any and all ranges in between to particular amounts. Further, it appears that disparate sections of the specification have been used to come up with the ranges recited in the claims. It is noted that claims 173-176 depend from claims 1,13,23,53 respectively. However, one would not have necessarily recognized the use of the instantly claimed ranges for applications of claims 1,13,23,53.

For at least these reasons, one would not conclude that the specification provides adequate support for Claims 136,173-176.

Response to Arguments Written Description New Matter

Applicants argue (pages 20-21,25) that the reference discloses lactated Ringers intravenous vehicles as well as polyalkylene glycols.

Applicants argue that since certain dosages work then one would recognize ranges.

Applicant's arguments filed 8/31/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 20-21) that the reference discloses lactated Ringers intravenous vehicles as well as polyalkylene glycols, the claims recite 'lactated Ringer's intravenous polyalklene glycol'. The disclosure of lactated Ringers intravenous vehicles is generic and would not lead one to polyalklene glycol. Although polyalklene glycol is mentioned, it is from a disparate section of the reference and there is no reason to read in that polyalklene glycol is intended to be lactated Ringer's intravenous polyalklene glycol.

Although argue that since certain dosages work then one would recognize ranges, disparate sections of the specification have been used to come up with the ranges recited in the claims. A disclosure of 2 data points does not lead one to any and all ranges in between those data points.

Claim Rejections - 35 USC § 102

The rejection based on Mann is maintained from the previous office action. Since the claims have been updated the rejection has been updated to correspond to the instant claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are rejected under 35 U.S.C. 102(e) as being anticipated by Mann (US 6,030,948). It is noted

that the 102(e) date for Mann is Dec. 19, 1997 based on MPEP section 706.02(f)(1) section III for a patent that is not from an international application and in which there is no international application in the continuity chain.

Mann teach a composition (claim 1, Tables 13-16) containing thymosin fraction 5. The thymosin fraction 5 includes both thymosin β4 (which comprises the sequence LKKTET) and thymosin α1 (which itself can augment the wound healing process – see page 11 of specification of the current invention thus meeting the limitation of claim 3 for example).

Claim 8 of Mann also teaches combinations of thymosin α1 and thymosin β4 thus meeting the composition limitations recited in claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 of the instant invention.

Mann teach a method of applying this composition to the scalp (claim 8). Prior to application to the scalp, an acid peel (i.e. chemical peel) solution is applied to the scalp and then removed. As such there is a reasonable basis that the removal of an acid peel solution would result in the removal of an outer layer of the skin and result in abrasion/damage/lesions/wounds on the skin. Mann teach that the composition can be applied topically as a lotion or gel (column 3 lines 52-63, thus meeting the limitations of claims 5-7 for example) and can be used for males or females (Tables 13-16). Since the composition is applied to the skin it is applied to a tissue and specifically to epithelial cells thus meeting the patient population of claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 of the instant invention.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the

> recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

It is noted that claim 136 recites 'an excipient or a composition'. As such, the claim is not limited to the recited compositions as the claim is open to an excipient. Further, Mann teach alcohols such as phenoxyethanol (table 14). It is noted that claims 173-175 recite ranges which include up to t 60 ug per 300ul (i.e. 200000 ng/ml). In the instant case, the Office has no facility to test the concentration of the thmyosin beta 4 in the thymosin fraction as shown in the tables of Mann. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements.

Response to Arguments 102 Mann

Applicants argue (pages 26-28) that Mann does not disclose that the acid peel is abrasive.

Applicants argue that the phrase 'acid peel' does not refer to any treatment intended to cause wounding to the living skin.

Applicants argue that acid peels cause the outer dead layers to peel away.

Applicants refer to another reference and amounts of TF5 used therein.

Applicants argue that it is not reasonable to interpret tissue injury to encompass removal of dead skin cells.

Applicants argue that the office stated that claims do not require the subject to have a wound.

Applicants argue that the declaration filed Sept 17,2008 overcomes any rejection of the claims.

Applicants argue that it is common knowledge that the purpose of acid peels it to beautify skin.

Applicants argue that the prior art recognize certain acid peels as mild.

Applicant's arguments filed 8/31/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 26-28) that Mann does not disclose that the acid peel is abrasive, the word abrasive is not used in the instant claims. Thus, whether or not the acid peel is abrasive is not necessarily relevant to the rejection.

Although Applicants argue that the phrase 'acid peel' does not refer to any treatment intended to cause wounding to the living skin, an anticipation rejection in the instant case is based on the active method steps not the intent. An intent is not an active method step.

Although Applicants argue that acid peels cause the outer dead layers to peel away, such statement is consistent with recognized definitions of wounds. First, it is noted that the instant claims do not distinguish dead skin from alive skin. Thus the term 'skin' is interpreted to include skin, both dead and alive. There is no basis to exclude certain types of skin from the genus of skin. Although not relied upon in the rejection, it is noted that TheFreeDictionary (The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages) teach that a wound involves the skin or another external surface being torn, pierced, cut, or otherwise broken (page 1). In the instant case, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. Since applicants are of the position (page 26 line 22) that acid peels peel away skin such interpretation seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken'. In other words it is unclear how skin can be removed if it is not broken away from other skin. Further, it is noted that the specification suggests a broad interpretation of the word 'wound'. In the instant case, claims 133-134,185-186 are evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in claim 133. Thus the broadest reasonable interpretation of 'wound' is consistent with the broad disclosure of the specification and dictionary definitions (see MPEP section 2111).

Although Applicants refer to another reference and amounts of TF5 used therein, the Office has no facility to test the concentration of the thymosin beta 4 in the thymosin fraction as shown in the tables of Mann. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). Such information provided by the applicant is not sufficient to overcome the rejection as it does not show a different between the products used.

Although Applicants argue that it is not reasonable to interpret tissue injury to encompass removal of dead skin cells, it is noted that the word injury does not appear in claim 1,13,,23,53, for example. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Although claim 185 recites injury claim 185 expressly recites that the injury is associated with a skin wound. Claim 186 expressly recites that the injury is associated with a skin wound. Thus, it is reasonable to interpret injury to encompass injuries associated with a skin wound since claim 186 expressly recites such. Although not relied upon in the rejection, it is noted that TheFreeDictionary (The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages) teach that a wound involves the skin or another external surface being torn, pierced, cut, or otherwise broken (page

1). In the instant case, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. Since applicants are of the position (page 26 line 22) that acid peels peel away skin such interpretation seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken'. In other words it is unclear how skin can be removed if it is not broken away from other skin. Further, it is noted that the specification suggests a broad interpretation of the word 'wound'. In the instant case, claims 133-134,185-186 are evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in claim 133. Thus the broadest reasonable interpretation is consistent with the broad disclosure of the specification and dictionary definitions.

Although Applicants argue that the office stated that claims do not require the subject to have a wound, claim 186 previously recited preventing. However the claim is still rejected because the claim refers to treating a subject with a tissue injury associated with a skin wound. Although not relied upon in the rejection, it is noted that TheFreeDictionary (The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages) teach that a wound involves the skin or another external surface being torn, pierced, cut, or otherwise broken (page 1). In the instant case, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. Since applicants are of the position (page 26 line 22) that acid peels peel away skin such interpretation seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken'. In other words it is unclear how skin can be removed if it is not broken away from other skin. Further, it is noted that the specification

suggests a broad interpretation of the word 'wound'. In the instant case, claims 133-134,185-186 are evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in claim 133. Thus the broadest reasonable interpretation is consistent with the broad disclosure of the specification and dictionary definitions.

Although Applicants argue that the declaration filed Sept 17,2008 overcomes any rejection of the claims, as set forth in the previous office action the declaration under 37 CFR 1.132 filed 9/17/08 is insufficient to overcome the rejection of claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 based upon a rejection under 35 U.S.C. 102(e) as being anticipated by Mann (US 6,030,948). As set forth previously, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. In the instant case, claim 133 is evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in claim 133. Section 716.01(c) of the MPEP states: 'In assessing the probative value of an expert opinion, the examiner must consider the nature of the matter sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985), cert. denied, 475 U.S. 1017 (1986).' In the instant case, the expert is of the opinion that that any person skilled in the art would recognize that surface acting peels do not cause abrasion/damage/lesions/wounds on skin. However, specific facts or data or references to support such a conclusion are not convincingly set forth. It is noted that the declaration refers to Table 10 of Mann. Although the expert asserts

and concludes that such composition would have certain properties, no experimental or documentary evidence has been provided. As quoted above section 716.01(c) of the MPEP states that the interest of the expert in the outcome is a factor to consider. In the instant case, Regenerx Corporate Presentation (retrieved from http://www.regenerx.com/pdf/NCInvestorPresentation_v38.ppt on 4/13/09 34 pages) teach that (page 32) Jo-David Fine, the expert listed in the declaration, is an advisor for the company Regenerx whose founder (page 31-32) is one of the inventors of the instant invention. As such, there is a reasonable basis that the expert has an interest in the outcome. In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence fails to outweigh the evidence of record. Further, although not relied upon in the rejection, it is noted that TheFreeDictionary (The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages) teach that a wound involves the skin or another external surface being torn, pierced, cut, or otherwise broken (page 1). In the instant case, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. Since applicants are of the position (page 26 line 22) that acid peels peel away skin such interpretation seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken'. In other words it is unclear how skin can be removed if it is not broken away from other skin. Further, it is noted that the specification suggests a broad interpretation of the word 'wound'. In the instant case, claims 133-134,185-186 are evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in

claim 133. Thus the broadest reasonable interpretation is consistent with the broad disclosure of the specification and dictionary definitions.

Although Applicants argue that it is common knowledge that the purpose of acid peels it to beautify skin, an anticipation rejection in the instant case is based on the active method steps not the intent. An intent is not an active method step. In the instant case, claim 53 the active step is contacting epithelial cells with a particular agent. Since Mann teach the active step the claim limitations are met.

Although Applicants argue that the prior art recognize certain acid peels as mild, an anticipation rejection in the instant case is based on the active method. In the instant case, claim 53 the active step is contacting epithelial cells with a particular agent. Since Mann teach the active step the claim limitations are met. Although not relied upon in the rejection, it is noted that TheFreeDictionary (The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages) teach that a wound involves the skin or another external surface being torn, pierced, cut, or otherwise broken (page 1). In the instant case, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. Since applicants are of the position (page 26 line 22) that acid peels peel away skin such interpretation seems to be reasonably within the realm of 'being torn,pierced,cut, or otherwise broken'. In other words it is unclear how skin can be removed if it is not broken away from other skin. Further, it is noted that the specification suggests a broad interpretation of the word 'wound'. In the instant case, claims 133-134,185-186 are evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in

claim 133. Thus the broadest reasonable interpretation is consistent with the broad disclosure of the specification and dictionary definitions.

The below 102b rejection is a new rejection necessitated by applicants amendments. First, the unclear amendments to claims 1,23 (see 112 2nd) have necessitated a new search. The previous search of 'isoform' is separate and distinct from the instant isoforms as claimed. Further, since applicants have provided Table 1 to clarify the scope of the claims (see previous 112 2nd rejection) such changes have necessitated a new search which uncovered the art cited below. In other words the previous office action (pages 9-10 of the 4/29/09 office action) clearly set forth that the isoforms were unclear. Although certain isoforms remain unclear (see new 112 2nd based on the amendments of claims 1,23) the claim amendments have necessitated a new search since at least some of the isoforms have been more specifically identified.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3,5-7,11,13-14,16-18,22-25,27,29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are rejected under 35 U.S.C. 102(b) as being anticipated by Turischev (Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' v45 (1996) pages 42-43).

It is noted that Turischev is in a non-English language. A translated version of the article is provided and will be relied upon and referenced to herein (Turischev translation of Farmatsiya 'Examining the effects of thymosin on the healing of flat cutaneous wounds in rats' total of 7 pages including the cover page)

Turischev teach the effect of thymosin on the healing of flat skin wounds in rats (title). Turischev teach that Thymosin (5th fraction) was used in the experiments (page 1 last paragraph). Turischev teach that the composition was administered intraperitoneally or topically to rats with wounds (page 2). Turischev teach that there is clear acceleration of the healing rates and that a dose of 0.8 ug accelerated wound healing (page 3).

Since Turischev teach rats with wounds the patient population of claims 1,13,23,25,27,38-39,53-55,133-134,185-186 are met. Since Turischev teach that the composition was administered intraperitoneally or topically via a solution (page 2) the limitations of claims 5-7,16-18,33-35,57-59,61,135,136 are met. Turischev teach that Thymosin (5th fraction) was used in the experiments (page 1 last paragraph). There is a reasonable basis that such composition contains thymosin beta 4 (compare Mann US 6,030,948 which is already of record) or an isoform and other components as recited in the claims, absence evidence to the contrary. A such, the composition limitations of claims 2-3,11,14,22,24,29,54,57-59 are met.

It is noted that claims 173-176,183-184 refer to properties or amounts. In the instant case, the Office has no facility to test such variables. Please note, since the Office does not have the facilities for examining and comparing Applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA

1977) and *In re Fitzgerald*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980), and "as a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements. Due to the lack of clarity an updated art search was performed.

Claim Rejections - 35 USC § 103

The 103 rejections are maintained from the previous office action. Since the claims have been updated the rejections have been updated to correspond to the instant claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3,5-8,11,13-14,16-19,22-29,33-36,38-39,53-55,57-61,133-136,173-176,183-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mann (US 6,030,948).

As discussed above, Mann teach methods of administering a composition comprising thymosin β4. Mann does not expressly teach the use of a recombinant or synthetic TB4 as in claims 8,19; the in vitro use as in claim 60; the use of sterile water as in claim 136.

Mann does expressly teach the use of thymosin beta 4 (claim 8). Since recombinant expression and purification of proteins is well-known in the art one of skill in the art would have been motivated to substitute the thymus purified peptide as taught by Mann with a recombinant

or synthetic peptide while maintaining an expectation of predictable results since the primary sequence of the protein is retained. Thus Mann obviates claims 8,19 of the instant invention.

Mann expressly teach the use of a vehicle (Tables 14-16) for the compositions. Since maintaining a pure, uncontaminated product is a goal one would be motivated to use sterile water as a specific vehicle while maintaining an expectation of predictable results since the same active ingredients are used. Thus Mann obviates claim 136 of the instant invention

Mann recognizes the use of in vitro experiments (Table 1). It would be obvious to one of skill in the art to determine if similar results could be obtained *in vitro* so that experimental results could be achieved in a more cost effective manner in a laboratory setting instead of requiring human subjects. Thus Mann obviates claim 60 of the instant invention.

From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

Claims 1-2,5-8,11,13,16-19,23-28,33-35,38-39,53-55,57-61,133-136,173-176,183-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page).

Malinda teach that Thymosin beta 4 (TB4) acts as a chemoattractant for endothelial cells (abstract). Malinda teach that in vitro wound closure is more rapid in the presence of TB4 (page 477). Malinda teach that cell migration is enhanced by TB4 (page 478). Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480).

Malinda does not expressly teach administration of TB4 to patients in need of wound healing.

Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that

TB4 could play a major role in would healing (page 480). Malinda recognizes the use of in vivo experiments (abstract). Since Malinda teach positive results for the in vitro studies (see wound closure model page 477) one would be motivated to use the method in vivo.

Further, Baumann (Table II page 21) also teach that TB4 leads to an increase in wound healing in vitro.

Further, Biotech Patent News teach that investigators will use thymosin beta 4 (last paragraph) in a wound healing study.

Taken together, the prior art clearly recognizes the use of TB4 for wound healing. Although the references do not expressly teach in a single embodiment the use for patients in need thereof one would be motivated to use TB4 in patients based on the promising in vitro results. One would have a reasonable expectation of success based on the in vitro results reported in the prior art.

Since Biotech patent news teach the use in wound healing studies one would be motivated to use TB4 specifically for those with wounds. Since Malinda teach the use of a scratch wound closure assay (page 475) one would be motivated to use TB4 in vivo for skin wounds. In order to use the TB4 for skin wounds one would be motivated to prepare the TB4 with an appropriate excipient such as water and an appropriate form such as a lotion for administration to the skin. Since in vitro models are used as a precursor to use in humans one would be motivated to use the methods on humans and apply TB4 to skin cells including epithelial cells (see page 474 of Malinda) based on the promising in vitro results. Although Malinda does not recite the source of the protein one would recognize that recombinant or synthetic production is a well known method in the art for production of peptides. Thus taken

together the references obviate the use of a specific agent (thymosin beta 4) which reads on the polypeptide as recited in the instant claims; the references motivate a specific use (wound healing) which motivates specific excipients, forms, and locations of administration as recited in the instant claims.

Further, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g.doses), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2144.05).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

Claims 1-8,11,13-19,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malinda et al (Faseb Journal 1997 cited in IDS 5/25/01) and Baumann et al 1997 (from 'Thymic peptides in preclinical and clinical medicine: an update:proceedings of the 2nd international thymus symposium' editor HR Maurer, pages 13-17) and Biotech Patent News (Dec 1 1997 1 page) and Puolakkainen et al (Journal of Surgical Research v58 1995 pages 321-329).

As discussed above, Malinda, Baumann, and Biotech Patent News obviate the use of TB4 for wound healing.

However, the references do not expressly teach in a single embodiment the use of a further agent (as recited in claims 3,14,22,29,36) or the use of TGF-beta (claims 4,15,30).

Puolakkainen recognize what is well-known in the art, that TGF-beta is known to enhance wound healing (title, page 325 discussion). Puolakkainen also recognize the optimization of the administration mode and dose and teach toward topical administration

(abstract and throughout). One would be motivated to use the teachings of Puolakkainen along with the other references since the references are drawn to methods of wound healing.

In the instant case, the claimed elements (thymosin beta 4, TGF-beta) were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Taken together the references meet the limitations of the instant claims. One would have a reasonable expectation of success since both references teach agents for wound healing.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements.

Section 2111.02 of the MPEP states:

> During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference (or, in the case of process claims, manipulative difference) between the claimed invention and the prior art. If so, the recitation serves to limit the claim. See, e.g., In re Otto, 312 F.2d 937, 938, 136 USPQ

458, 459 (CCPA 1963)

In the instant case, limitations such as promoting migration (claim 53) do not result in a manipulative difference and do not serve to limit the claims.

Response to Arguments 103 Mann

Applicants argue (pages 28-29) that there is no connection made between wound-healing and hair restoration.

Applicants argue that because Mann does not suggest the methods it does not render any of the dependent claims obvious.

Applicant's arguments filed 8/31/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 28-29) that there is no connection made between wound-healing and hair restoration the instant claims do not recite hair restoration. In the instant case, claim 53 the active step is contacting epithelial cells with a particular agent. Since Mann teach the active step the claim limitations are met. Although not relied upon in the rejection, it is noted that TheFreeDictionary (The FreeDictionary entry for 'wound' accessed from http://www.thefreedictionary.com/wound on 12/17/09, 7 pages) teach that a wound involves the skin or another external surface being torn, pierced, cut, or otherwise broken (page 1). In the instant case, it is noted that 'wound' is not specifically defined in the instant specification. As such, the claims are given the broadest reasonable interpretation in accord with section 2111 of the MPEP. Since applicants are of the position (page 26 line 22) that acid peels peel away skin such interpretation seems to be reasonably within the realm of 'being torn,pierced,cut, or

otherwise broken'. In other words it is unclear how skin can be removed if it is not broken away from other skin. Further, it is noted that the specification suggests a broad interpretation of the word 'wound'. In the instant case, claims 133-134,185-186 are evidence that the term 'wound' represents a genus of wounds that includes, for example, the many different wounds recited in claim 133. Thus the broadest reasonable interpretation is consistent with the broad disclosure of the specification and dictionary definitions.

Although Applicants argue that because Mann does not suggest the methods it does not render any of the dependent claims obvious, it is noted that a 102 rejection is separate and distinct from a 103 rejection. The arguments related to the 102 rejection are discussed above. Further, a 103 rejection does not require that the reference also be used in a 102 rejection.

Response to Arguments 103 Malinda et al

Applicants argue (pages 29-32) that the office has extrapolated in vitro studies.

Applicants argue that the disclosure of Malinda is theoretical at best.

Applicants argue that Baumann does not provide anything more than a guess.

Applicants argue that the Alpha 1 Biomedical abstract should be read in light as unverified and self-serving.

Applicants argue that the art does not provide a reasonable expectation that TB4 would work.

Applicants argue that Puolakkainen does not make up for the failure of the other references.

Applicant's arguments filed 8/31/09 have been fully considered but they are not persuasive.

Although Applicants argue (pages 29-32) that the office has extrapolated in vitro studies, it is first noted that the rejection is a 103 rejection and a such any single reference does not necessarily anticipate the claims. Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480). Malinda recognizes the use of in vivo experiments (abstract). Since Malinda teach positive results for the in vitro studies (see wound closure model page 477) one would be motivated to use the method in vivo. Further, Baumann (Table II page 21) also teach that TB4 leads to an increase in wound healing in vitro. Further, Biotech Patent News teach that investigators will use thymosin beta 4 (last paragraph) in a wound healing study. Taken together, the prior art clearly recognizes the use of TB4 for wound healing. Although the references do not expressly teach in a single embodiment the use for patients in need thereof one would be motivated to use TB4 in patients based on the promising in vitro results. One would have a reasonable expectation of success based on the in vitro results reported in the prior art. Further, section 2143.02 of the MPEP II states that obviousness does not require absolute predictability. In the instant case, the in vitro results taught by the references provide at least some degree of predictability.

Although Applicants argue that the disclosure of Malinda is theoretical at best, Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480). Malinda teach positive results for the in vitro studies

(see wound closure model page 477). Section 2143 of the MPEP states that suggestions of the prior art may support conclusions of obviousness. As such, whether or not a reference is theoretical does not exclude any particular reference. There is no requirement that a reference must reduce to practice.

Although Applicants argue that Baumann does not provide anything more than a guess, Section 2143 of the MPEP states that suggestions of the prior art may support conclusions of obviousness. Further, Baumann (Table II page 21) also teach that TB4 leads to an increase in wound healing in vitro. Such data is factual evidence, not a guess. Further, section 2121 of the MPEP states that prior art is presumed enabling. Further, section 2143.02 of the MPEP II states that obviousness does not require absolute predictability.

Although Applicants argue that the Alpha 1 Biomedical abstract should be read in light as unverified and self-serving, section 2121 of the MPEP states that prior art is presumed enabling. There is no reason to exclude the article as a prior art reference.

Although Applicants argue that the art does not provide a reasonable expectation that TB4 would work, Malinda teach that TB4 is important in angiogenesis and that the formation of blood vessels is an important part of wound healing (page 480). Malinda teach that others report that TB4 could play a major role in would healing (page 480). Malinda recognizes the use of in vivo experiments (abstract). Since Malinda teach positive results for the in vitro studies (see wound closure model page 477) one would be motivated to use the method in vivo. Further, Baumann (Table II page 21) also teach that TB4 leads to an increase in wound healing in vitro. Further, Biotech Patent News teach that investigators will use thymosin beta 4 (last paragraph) in a wound healing study. Taken together, the prior art clearly recognizes the use of TB4 for wound

healing. Although the references do not expressly teach in a single embodiment the use for patients in need thereof one would be motivated to use TB4 in patients based on the promising in vitro results. One would have a reasonable expectation of success based on the in vitro results reported in the prior art. Further, section 2143.02 of the MPEP II states that obviousness does not require absolute predictability. In the instant case, the in vitro results taught by the references provide at least some degree of predictability.

Double Patenting

The double patenting rejections are maintained from the previous office action. Since the claims have been updated the rejections have been updated to correspond to the instant claims.

The terminal disclaimer filed on 9/17/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 7,268,118 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on 9/17/08 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on 11/284,430 has been reviewed and is accepted. The terminal disclaimer has been recorded.

It is noted that 10/714,405 has been abandoned.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8,11,13-19,22-30,33-36,38-39,53-55,57-61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7-16,29-47 of copending Application No. 11/284,408 ('408). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '408 application teaches methods of administering compositions to the skin comprising thymosin beta four (for example, claim 7), transforming growth factor (claim 8), for topical treatment (for example, claim 7). '408 teach the administration to skin specifically damaged skin (claim 29) and specifically to epithethial tissue (claim 38). '408 teach doses (claim 38,29) that meet the limitations of the instant claims.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-23,26 of copending Application No. 11/917,869 ('869). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '869 application teaches methods of administering compositions to the skin comprising thymosin beta four isoform or LKKTET (for example, claim 13,21), and specific doses (claim 23) as in the instant claims.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-32 of copending Application No. 11/715,997 ('997). Although the conflicting claims are not identical, they are not patentably distinct from each other

because the '997 application teaches methods of administering compositions to the skin comprising thymosin beta four or LKKTET (for example, claim 21), and specific doses (claim 27) as in the instant claims.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-3,5-7,11,13-14,16-18,22-29,33-36,38-39,53-55,57-59,61,133-136,173-176,183-186 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 12/444,331 ('331). Although the conflicting claims are not identical, they are not patentably distinct from each other because the '331 application teaches methods of administering compositions to the skin comprising thymosin beta four or LKKTET (for example, claim 1), and specific doses (claim 7) as in the instant claims.

Although unclear (see 112 2nd) the claims are given the broadest reasonable interpretation. In the instant case, it is difficult to ascertain the scope of the claim. It is possible that there was some type of typographical error, but it is unclear if there are missing words or if incorrect words were used. For purposes of examination, the phrase 'replaced with another

hydrophobic amino and residue' is interpreted such that the phrase does not include new matter and complies with the written description requirements.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 11/715,997 and 12/444,331; discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Response to Arguments double patenting

Applicants request (pages 32-33) that the rejections be held in abeyance.

Applicant's arguments filed 8/31/09 have been fully considered but they are not persuasive.

Although Applicants request (pages 32-33) that the rejections be held in abeyance, such request does not overcome the rejection. The instant claims are not allowable.

Conclusion

The 112 2nd rejections are new rejections based on applicants amendments.

The above 102b rejection is a new rejection necessitated by applicants amendments. First, the unclear amendments to claims 1,23 (see 112 2nd) have necessitated a new search. The previous search of 'isoform' is separate and distinct from the instant isoforms as claimed. Further, since applicants have provided Table 1 to clarify the scope of the claims (see previous 112 2nd rejection) such changes have necessitated a new search which uncovered the art cited below. In other words (pages 9-10 of the 4/29/09 office action) the previous office action clearly set forth that the isoforms were unclear. Although certain isoforms remain unclear (see new 112 2nd based on the amendments of claims 1,23) the claim amendments have necessitated a new search since at least some of the isoforms have been more specifically identified.

The new matter, 102e,103, and double patenting rejections are based on rejections set forth in the previous office action. Thus applicants amendments have necessitated any new grounds of rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654